Citation:

China Salt Substitute Study Collaborative Group. Salt substitution: A low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial. *J Hypertens.* 2007 Oct; 25 (10): 2,011-2,018.

PubMed ID: 17885542

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effects of using salt substitutes instead of salt on blood pressure (BP) of a rural Northern Chinese population.

Inclusion Criteria:

- Diagnosis of coronary cerebral disease
- Diagnosis of coronary vascular disease
- Diagnosis of diabetes
- Diagnosis of renal impairment
- Use of potassium-sparing medications
- ≥55 years of age
- Systolic blood pressure (SBP) of ≥160mmHg
- Estimated sodium intake of ≥260mmol per day
- Receptive to the possibility of replacing sodium intake with a salt substitute
- No known indication or contraindication of replacing sodium intake with a salt substitute by the participant
- No known indication or contraindication of replacing sodium intake with a salt substitute by the participants' fellow household members
- Normal serum potassium before and after run-in period
- Normal serum creatinine before and after run-in period.

Exclusion Criteria:

- Abnormal serum potassium before and after run-in period
- Abnormal serum creatinine before and after run-in period
- Any known indication or contraindication of replacing sodium intake with a salt substitute by the participant, including the use of potassium-sparing medications or significant renal

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impairment
- Any known indication or contraindication of replacing sodium intake with a salt substitute by the participants' fellow household members.

Description of Study Protocol:

Recruitment

Patients seen for routine check-ups done between May 2004 to August 2005 at 39 sites distributed between six regional coordinating centers in Northern China (Hejlongjoang, Tianjin, Liaoning, Shanxi and two centers in Beijing) were potentially eligible for the study, if they had a high risk of future vascular disease based on a doctor's diagnosis.

Design

- Randomized, double-blinded, controlled trial
- Randomization was done using a central computerized randomization service accessed by Centrex physicians via the study Website.

Blinding Used

Study salt bags were identical except for a three-digit code corresponding to the randomization number.

Intervention

- Subjects were provided with up to 3kg of salt (100% sodium chloride) or reduced-sodium, high-potassium salt substitute (65% sodium chloride, 25% potassium chloride and 10% magnesium sulphate) for 12 months
- The randomized treatment was delivered in increments of 1kg bags based on determined need of the household. Participants were instructed to use the study salt for "all cooking, pickling and other uses within the household"
- Existing salt and foods previously pickled in salt were not removed from the participants' households.

Statistical Analysis

- The study was designed to provide 90% power at P=0.05 to detect 3.1 to 1.7mmHg or greater difference between randomized groups in mean casual follow-up BP levels. This assumed that usual sodium intake in study participants was about 50mmol per 24 hours. The anticipated minimum mean decrease in dietary sodium intake was about 45mmol per 24 hours (17%) and the anticipated minimum increase in dietary potassium intake was 22mmol per 24 hours (44%)
- Mean levels and proportions were calculated for baseline and follow-up characteristics
- Analysis of treatment effects was by intention to treat with between group comparisons for the primary outcome to fit mixed linear models for repeated measures ANOVA.

Data Collection Summary:

Timing of Measurements

- Monthly: Subjects were provided with up to 3kg of salt (100% sodium chloride) or salt

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substitute (65% sodium chloride, 25% potassium chloride and 10% magnesium sulphate) for 12 months
- At one, two, three, six, nine and 12 months: Compliance was determined by a self-reported response of 'all,' 'nearly all,' 'half,' 'less that half' or 'none'
- Before and after the run-in period: Blood tests were done measuring serum creatinine and potassium were taken to ensure inclusion criteria was met
- At baseline, one, six and 12 months: Surveys were completed regarding the three aspects of "the taste of home-cooked food"
- At baseline, one, six and 12 months: "Salty soup" was given in an effort to define any change in the preferred level of saltiness over time.

Dependent Variables

- Blood pressure was measured with Omron sphygmomanometer
- Urinary sodium and potassium measured using ion selective electrode method or atomic absorption spectrophotometry.

Independent Variables

- Subjects were provided with up to 3kg of salt (100% sodium chloride) or reduced-sodium, high-potassium salt substitute (65% sodium chloride, 25% potassium chloride and 10% magnesium sulphate) for 12 months
- The randomized treatment was delivered in increments of 1kg bags based on determined need of the household. Participants were instructed to use the study salt for "all cooking, pickling and other uses within the household"
- Existing salt and foods previously pickled in salt were not removed from the participants households
- Compliance was determined by a self-reported response of 'all,' 'nearly all,' 'half,' 'less that half' or 'none.' "The taste of home-cooked food" was measured using 100mm visual analogue scales for saltiness (not at all salty to very salty), flavor (very weak to very strong) and overall liking (dislike extremely to like extremely). "Salty soup" was given in an effort to define any change in the preferred level of saltiness over time.

Control Variables

- Body mass index (BMI)
- Age
- Baseline anticoagulant use.

Description of Actual Data Sample:

- *Initial N:* 700 commenced run-in and 608 were randomized (268 males, 340 females)
    - Salt substitute: 166 females, 140 males
    - Salt: 174 females, 128 males
- *Attrition (final N):* 585 subjects.
    - Salt substitute: 292
    - Salt: 293
- *Mean age:*
    - Salt Substitute: 59 years old
    - Salt: 61 years old
- *Ethnicity:* 100% Chinese

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- Other relevant demographics:
  - Treated diabetes and age >55 years:
    - Salt substitute: 48 (16%)
    - Salt: 57 (19%)
  - Antihypertensive medications:
    - Salt substitute: 185 (61%)
    - Salt: 184 (61%)
  - Mean BP (mmHg):
    - Salt substitute 159/93 (25/14)
    - Salt 159/93 (26/14)
- *Anthropometrics:* BMI:
  - Salt substitute: Mean 26kg/m^2
  - Salt: Mean 25 kg/m^2
  - Baseline characteristics were balanced between groups except for BMI, age and baseline anticoagulant use
- *Location:* Rural Northern China.

Summary of Results:

Key Findings

- Mean overall difference in SBP between randomized groups was 3.7mmHg (95% CI: 1.6 to 5.9, P<0.001)
- SBP was significantly lower in the salt substitute group than in the normal salt group at the six- , nine- and 12-month visits (all P<0.02)
- There was strong evidence that the magnitude of this reduction increased over time (P=0.001) with the maximum net reduction of 5.4mmHg (2.3 to 8.5) achieved at 12 months
- There were no detectable effects on DBP at any time point or overall, and no evidence of any evolution of a difference over time.

Other Findings

- The analyses done to explore possible interactions of the effects of randomized treatment with participant characteristics identified no effects of baseline age, sex, history of cardiovascular disease, urinary sodium or potassium concentrations or ratio of sodium to potassium concentrations on mean follow-up SBP (all P for heterogeneity higher than 0.07)
- There were no changes over time in either group or differences between randomized groups in the perception of food taste, in terms of saltiness, liking or overall acceptability (all P>0.3)
- There were no changes over time in either group or differences between randomized groups in the evaluations of the soup provided at follow-up visits (all P>0.09)
- There were no detectable differences in occurrence of serious adverse events between randomized groups (all P>0.4), and no episodes of severe hyperkalemia recorded.

Author Conclusion:

Salt substitution produced a substantial and sustained SBP reduction in this population, and should be actively promoted as a low-cost alternate or adjunct to drug therapy for people consuming significant quantities of salt.

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Reviewer Comments:

- *Reasonably large sample size, careful measurement of BP*
- *Baseline characteristics were balanced between groups except for BMI, age and baseline anticoagulant use, but these were controlled for in the statistical analysis.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes

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3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes

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6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes

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	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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